

I. Amendments:

Amendment to the Specification:

The specification has been amended as follows: Underlines indicate insertions and ~~strikeouts~~ indicate deletions.

Please replace paragraph [0013] with the following amended paragraph:

“DPP IV cleaves the ~~Ala-Asp~~ Ala-Glu bond of the major circulating form of human GLP-1 (human GLP-1 (7-36) NH₂: His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-NH₂), releasing an N-terminal dipeptide.”

Please replace paragraph [0024] with the following amended paragraph:

“X-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-~~val~~ Val-Lys-Gly-Arg-Y (SEQ ID NO.1)”

Please replace paragraph [0037] with the following amended paragraph:

“The present invention further relates to a method of treating a disease or condition associated with a disorder of glucose metabolism. The invention, in yet another embodiment relates to a prevention (e.g. prophylaxis) of a disease or condition associated with glucose metabolism. Non-limiting examples of glucose disorders include: diabetes mellitus of Type I or Type II, or insulin resistance, weight disorders and diseases or conditions associated thereto, wherein such weight disorders or associated conditions include obesity, overweight-associated conditions, satiety deregulation, reduced plasma insulin levels, increased blood glucose levels, or reduced pancreatic beta cell mass.”

Please replace paragraph [0038] with the following amended paragraph:

“In one embodiment, the present invention relates to a method for treating diabetes mellitus of Type I or Type II, comprising the step of administering to a subject in need of such treatment a

therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof.

Please replace paragraph [0039] with the following amended paragraph:

“In a second embodiment, the present invention relates to a method for treating insulin resistance, comprising the step of administering to a subject in need of such treatment a therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof.”

Please replace paragraph [0040] with the following amended paragraph:

“In a third embodiment, the present invention relates to a method for weight lowering of a subject, comprising the step of administering ~~an~~ therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof, to the subject.”

Please replace paragraph [0041] with the following amended paragraph:

“In a fourth embodiment, the present invention relates to a method for reducing satiety of a subject, comprising the step of administering a therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof to the subject ~~in need thereof~~.”

Please replace paragraph [0042] with the following amended paragraph:

“In a fifth embodiment, the present invention relates to a method for post-prandially increasing plasma insulin levels in a subject, comprising the step of administering a therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof, to the subject.”

Please replace paragraph [0043] with the following amended paragraph:

“In a sixth embodiment, the present invention relates to a method for reducing fasting blood glucose levels in a subject, comprising the step of administering a therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof, to the subject.”

Please replace paragraph [0044] with the following amended paragraph:

“In a ~~seventy~~ seventh embodiment, the present invention relates to a method for increasing pancreatic beta cell mass in a subject, comprising the step of administering a therapeutically effective amount of ~~the~~ a peptide of the present invention, or a pharmaceutically acceptable salt thereof to the subject.”

Please replace paragraph [0047] with the following amended paragraph:

“The present invention further relates to a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for treating diabetes mellitus of Type I or Type II in a subject.”

Please replace paragraph [0048] with the following amended paragraph:

“The present invention further relates to a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for treating insulin resistance in a subject.”

Please replace paragraph [0049] with the following amended paragraph:

“The present invention further relates to a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for lowering weight of a subject.”

Please replace paragraph [0050] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for reducing satiety of a subject.”

Please replace paragraph [0051] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for post-prandially increasing plasma insulin levels in a subject.”

Please replace paragraph [0052] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for reducing fasting blood glucose level in a subject.”

Please replace paragraph [0053] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for increasing pancreatic beta cell mass in a subject.”

Please replace paragraph [0054] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for treating diabetes mellitus of Type I or Type II in a subject.”

Please replace paragraph [0055] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for treating insulin resistance in a subject.”

Please replace paragraph [0056] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for lowering weight of a subject.”

Please replace paragraph [0057] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for increasing satiety of a subject.”

Please replace paragraph [0058] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for post-prandially increasing plasma insulin levels in a subject.”

Please replace paragraph [0059] with the following amended paragraph:

“The present invention further relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for reducing fasting blood glucose levels in a subject.”

Please replace paragraph [0060] with the following amended paragraph:

“Finally, the present invention relates to ~~the~~ a use of the peptides of the present invention, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for increasing pancreatic beta cell mass in a subject.”

Please replace paragraph [0074] with the following amended paragraph:

“As used herein, the term “rigidifying hydrophobic moiety” is intended to mean a conformationally rigid moiety, which has a limited number of spatial orientations due to the presence of one or more rigidifying elements in its backbone such as, a double bond, a triple bond, or a saturated or unsaturated ring, which have little or no conformational mobility. As a result, the number of conformers or rotational isomers is reduced when compared to the corresponding straight, or unsubstituted and saturated aliphatic chain. These rigidifying hydrophobic moieties are derived from carboxylic acids which can be divided into the following groups:”

Please replace the paragraph of the title of Example 1 at page 22, with the following paragraph:

“Solid phase synthesis of GLP-1 (7-37)COOH or GLP-1 (7-~~37~~36)CONH₂ and coupling of rigid hydrophobic moieties”

Please replace Table 2 of Example 1 at page 24, with the following Table 2:

Compound	Description of GLP-1 peptide
Wild type	GLP-1 (7-37) OH
1	[H7] diphenylacetic acid GLP-1 (7-37) COOH
2	[H7] O-tolylacetic acid GLP-1 (7-37) COOH
3	[H7] α -phenyl O-toluic acid GLP-1 (7-37) COOH
4	[H7] (+,-) cis 2-ethylcyclopropyl acetic acid GLP-1 (7-37) COOH
5	[H7] 3-aminophenyl acetic acid GLP-1 (7-37) COOH
6	[H7] 2-ethoxybenzoic acid GLP-1 (7-37) COOH
7	[H7] 3-methoxyphenyl acetic acid GLP-1 (7-37) COOH
8	[H7] Salicylic acid GLP-1 (7-37) COOH
9	[H7] n-phenyl anthranilic acid GLP-1 (7-37) COOH
10	[H7] 3-(phenylthio)acrylic acid GLP-1 (7-37) COOH
11	[H7] 2,6-difluorophenyl acetic acid GLP-1 (7-37) COOH
12	[H7] 2,3,4,5,6-pentafluorophenyl acetic acid GLP-1 (7-37) COOH
13	[H7] 3-hydroxy phenyl acetic acid GLP-1 (7-37) COOH
14	[H7] (1R, 2R) 2-ethylcyclopropyl acetic acid GLP-1 (7-37) COOH
15	[H7] (1S, 2S) 2-ethylcyclopropyl acetic acid GLP-1 (7-37) COOH
16	[H7] 3-aminophenyl acetic acid GLP-1 (7-36) CONH ₂
17	[H7] Salicylic acid GLP-1 (7- 37 <u>36</u>) CONH ₂

Please replace the paragraph under Table 2 at page 24, with the following paragraph:

“GLP-1 analogues containing rigid hydrophobic moieties.”